

REMARKS**Amendments to the Claims**

All pending claims stand finally rejected except claim 10, which is allowed. Applicants cancel all pending claims and submit new claims 35-52. Cancellation of the previously pending claims has not been made in acquiescence to the outstanding rejections, but instead to better protect Applicants' transmucosal drug delivery product, currently in clinical trials before the US Food and Drug Administration. Applicants retain the right to pursue all cancelled subject matter in one or more continuing applications. New claims 35-52 are supported throughout the specification. *No new matter is added by the instant amendment.*

Request for Confirmation of Entry of Drawings

Applicants respectfully request acknowledgement that the amendment filed on December 22, 2006 has been entered. The amendment was in response to the *Ex Parte Quayle* action mailed August 27, 2006 requesting that Figures 1 and 2 be made of record.

Outstanding Rejections under 35 USC 103(a)

Previously pending claims 1-3, 5-8, 12, 15-18, and 33-34 were rejected as being obvious over US Patent No. 4,765,983 to Takayanagi *et al.* (Takayanagi), in view of US Patent No. 4,594,240 to Kawata *et al.* (Kawata), WO 95/05416 (WO '416), and EPA 250187 (EPA '187). All previously pending claims have been canceled without prejudice. Applicants, however, have carefully considered these rejections in light of new claims 35-52.

New claims 35-52 are directed to a transmucosal delivery device in the form of a bioerodabile flexible film for the systemic delivery of a pharmaceutical. The device includes bioerodabile mucoadhesive layer, a bioerodabile non-adhesive backing layer, and a systemic pharmaceutical incorporated into the flexible film. The transmucosal delivery device is thin, flexible and orally erodes such that there is an effective residence time with minimal or no foreign body sensation.

Takayanagi discloses adhesive medical tapes for the local delivery of antiphlogistic and analgesic medicaments to inflamed mucosal tissue. Takayanagi teaches that the tape includes a

support layer that is intestine soluble (*i.e.*, dissolvable in the intestines) so that the device, upon application to the affected tissue, provides both immediate and long lasting effect to the inflamed tissue.

In contrast, the invention as claimed is directed, in part, to a device for the transmucosal delivery of a systemic pharmaceutical, not to a device for the local delivery of, *e.g.*, anti-inflammatory agents to inflamed mucosal tissue. Furthermore, the claimed device is bioerodible and erodes in the oral cavity, as opposed to the device of Takayanagi that includes a support layer that must be swallowed or manually removed from the application site.

Kawata was cited in the Office action for teaching “the use of hydroxyethyl cellulose and polyacrylic acid in the flexible pharmaceutical containing sheet.” Kawata, however, fails to make up for the deficiencies of Takayanagi. Like Takayanagi, Kawata is directed to the local delivery of a medicament, specifically, prostaglandins for promoting tooth-movement in orthodontics. The device includes an active layer, which includes both water soluble and water insoluble polymers, and a base sheet. Exemplary base sheet materials are described at column 2, lines 25-31 of Kawata as follows:

The base sheet used in the present invention includes non-woven fabric made from nylon, vynylon, etc., lints, papers, polyvinyl chloride film, polyurethane film, ethylene-vinyl acetate copolymer film, or other synthetic polymer films, which are flexible.

The examples recite the use of a non-woven fabric as the base sheet. As taught, *e.g.*, in the paragraph at column 1, line 63 through column 2, line 2:

[I]t has been found that a preparation comprising a layer of a pharmaceutical composition containing a prostaglandin and a flexible base sheet is suitable because it can be retained within the oral cavity for a long period of time *without being affected with saliva* and further the prostaglandin contained therein can effectively be absorbed to promote the tooth-movement.
(emphasis added)

In fact, it appears that were the devices of Takayanagi or Kawata modified to erode in the oral cavity, this modification would render the devices unsuitable for their intended purpose of long lasting delivery of a local medicament (to treat inflammation or promote tooth-movement, respectively).

WO '416 also does not make up for the deficiencies of Takayanagi. WO'416 is generally directed to adhesive films that can be used for affixing prosthesis in a body cavity and/or controlled release of substances within the body cavity. *See e.g.*, the Abstract, Technical Field, and Summary of the Invention. Although release of a substance "transmucosally" is discussed (*see e.g.*, page 7, lines 4-7 and page 58, lines 3-18), the transmucosal delivery of a systemic pharmaceutical is neither disclosed nor exemplified. The only actives specifically discussed in regard to transmucosal transport are local agents. Specifically, in Examples XI-XV, it is demonstrated that only "very low values" of Dyclonine HCL and benzocaine (local agents for the relief of sore throat) are transported into the mucosal tissue by the exemplary devices.

Similar to WO '416, EP '187 generally discloses devices for oral delivery of breath fresheners or drugs into the oral cavity and/or locally to the mucosa.

Accordingly, Applicants respectfully submit new claims 35-52 are patentable in view of the cited references.

Outstanding Rejections under 35 USC 112, Second Paragraph

Previously pending claims 1-3, 5-9, 12-13, 15 and 34 were rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. All previously pending claims have been canceled without prejudice. Applicants have carefully considered these rejections in drafting new claims 35-52 and submit that new claims meet all of the requirements of 35 USC 112, second paragraph.

CONCLUSION

In view of the above amendment, Applicants believe that the pending application is in condition for allowance. The Examiner is invited to contact the undersigned with questions or comments with regard to the present application.

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